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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,085	05/11/2001	Akihiro Ishii	3007/49966	5264

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EXAMINER

ZUCKER, PAUL A

ART UNIT	PAPER NUMBER
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1621

DATE MAILED: 05/03/2002

11

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/853,085

Applicant(s)

ISHII ET AL.

Examiner

Paul A. Zucker

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☒ Claim(s) 1,5-8,10,12 and 13 is/are objected to.
- 8) ☒ Claim(s) 1-13 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All   b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: .

**DETAILED ACTION**

***Election/Restrictions***

1. Applicant's election without traverse of Group I, claims 1-13, in Paper No. 9 is acknowledged. Applicant has cancelled claims 14-24. Claims 1-13 remain outstanding.

***Oath/Declaration***

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because it does not identify the mailing or post office address of each inventor. A mailing or post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing or post office address should include the ZIP Code designation. The mailing or post office address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

***Specification***

3. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 5, 8 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 5, 8 and 10 recite limitations within parentheses. For example on lines 7-10 of claim 1. The use of parenthetical expressions renders the claim indefinite because it is unclear whether the limitation(s) contained within parentheses are part of the claimed invention. See MPEP § 2173.05(d).
5. Claims 1, 5, 8 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 5, 8 and 10 recite limitations "[Chemical #]" where # corresponds to a numerical designation in the specification. The claims may not make reference to the specification. In addition characterization of compounds with two numerical designations creates confusion. Claims 1, 5, 8 and 10 are therefore rendered indefinite.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1-9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bringman et al (DE 3819438-A1 01-1989) and further in view of Van Wagenen et al (US 6,211,244-B1 04-2001).

The instantly claimed invention consists of the synthesis of an optically active phenyl-substituted phenethylamine via the formation of the imine (Schiff's base) via reaction of a ketone and optically active phenethylamine, reduction of the imine with sodium borohydride, followed by hydrogenolysis to give the desired product. The instant invention claims fluorine and trifluoromethyl substitution on the substituted phenethylamine produced. A method of purification of the 2° amine intermediate is also claimed.

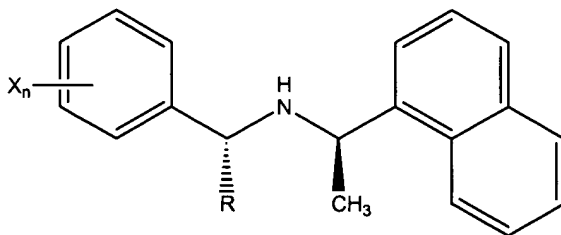
Bringman teaches (Page 2, line 65- page 3, line 46) the synthesis of an optically active phenyl-substituted phenethylamine via the formation of the imine (Schiff's base) by reaction of a ketone and optically active phenethylamine, reduction of the imine with hydrogen and a catalyst, followed by hydrogenolysis to give the desired

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product. Bringman further teaches (Page 3, lines 19-20) the hydrogenolysis of the 2° amine (reduced Schiff's base) at temperatures of 0-50 °C and pressures of 0-300 bar. Bringman exemplifies (Page 4, line 46 - Page 5, line 25; see Table experiment 10) the synthesis of the 2-fluorophenyl compound by hydrogenolysis of its acetate salt in methanol. The examiner notes that the corresponding processes that produce positional isomers about the phenyl ring are prima facie obvious over that taught by Bringman.

Bringman is silent with regard to the use of borohydride reducing agents to reduce the Schiff's base and with regard to trifluoromethyl substitution in the product.

Van Wagenen, however, teaches (Column 14, line 50 – column 15, line 12) a genus of compounds that have the structure of instant general formula [4]. Van Wagenen, teaches (Column 13, lines 11-25) a preferred embodiment of the following structure:



where  $n = 1-5$ ;  $X$  may be  $F$  or  $CF_3$ ; and  $R = H$  or  $CH_3$ . Where  $R = CH_3$  this structure then corresponds to the reduced Schiff's base intermediates of the instant claimed process. Van Wagenen further teaches (Column 30, lines 43-48) a general method of synthesis of these and related compound which proceeds through formation of a Schiff's base between a ketone and an amine and reduction to the 2° amine with sodium borohydride. Van Wagenen further teaches (Column 32, lines 20-38) that

compounds of the general structure taught can be converted to the hydrochloride salt and recrystallized as a method of purification.

Thus the instantly claimed invention would have been obvious to one of ordinary skill in the art. The motivation would have been to extend the utility of the process taught by Bringman to the synthesis of compounds for which the intermediates are taught by Van Wagenen. The process of Bringman is further improved by use of the borohydride reduction as taught by Van Wagenen. The expectation for success would have been near certitude since Van Wagenen teaches the intermediates required for the process of Bringman.

7. Claims 10, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hagitani et al (JP 09-278718 10-1997).

The instantly claimed invention is a method for the purification of optically active fluoro- and trifluoromethyl- substituted phenethylamines by formation of the corresponding mandelic or tartaric acid salt followed by recrystallization.

Hagitani teaches (Machine translation, page 5, lines 1-10) a method of purification of disubstituted phenethylamines which proceeds through formation and recrystallization of the mandelic acid salt. Hagitani further teaches (Machine translation, page 3, lines 30-33) disubstituted phenethylamines in which the substituents can be halo (fluoro) and fluoroalkyl (trifluoromethyl). Hagitani

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specifically teaches (Machine translation, page 3, line 42) 3-fluorophenyl substitution.

Thus the instantly claimed process would have obvious to one of ordinary skill in the art. The motivation would have been to apply the method for purification of disubstituted phenethylamines taught by Hagitani to the purification commercially important compounds. The expectation for success would be near certitude since Hagitani teaches that the instant compounds are within the scope of his invention.

### ***Conclusion***

8. Claims 1-13 are outstanding. Claims 1-13 are rejected. Claims 1,5, 6,7,8, 10, 12 and 13 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 703-306-0512. The examiner can normally be reached on Monday-Friday 7:00-3:30.

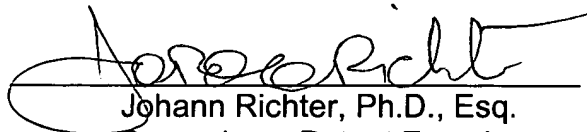
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 703-308-4532. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Paul A. Zucker  
Patent Examiner  
Technology Center 1600

May 2, 2002



Johann Richter, Ph.D., Esq.  
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